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     (FILE 'HOME' ENTERED AT 15:19:17 ON 19 OCT 2001)

     FILE 'HCAPLUS' ENTERED AT 15:20:31 ON 19 OCT 2001
                E GREEN FLUORESCENT PROTEIN/CT
                E E3+ALL
                E FLUORESCENT PROTEIN/CT
                E CLEAVAGE SITE/CT
                E PROTEASE CLEAVAGE SITE/CT
L1         43260 S (PROTEIN OR POLYPEPTIDE) (L) FLUORES?
L2           259 S L1 (L) (PROTEASE OR PROTEINASE) (L) CLEAV?
L3            11 S L2 (L) (LOOP OR SHEET)
L4             9 S L3 AND PD<19990418
                E CASPASE/CT
                E E3+ALL
L5            14 S L2 (L) CASPASE
L6             9 S L5 AND PD<19990418
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=> d ibib ab 1-9

L4 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:750197 HCAPLUS
DOCUMENT NUMBER: 132:46547
TITLE: Limited proteolysis of bovine .alpha.-lactalbumin: isolation and characterization of protein domains
AUTHOR(S): De Laureto, Patrizia Polverino; Scaramella, Elena; Frigo, Marta; Wondrich, Francesca Gefter; De Filippis, Vincenzo; Zambonin, Marcello; Fontana, Angelo
CORPORATE SOURCE: CRIBI Biotechnology Centre, University of Padua, Padua, 35121, Italy
SOURCE: Protein Sci. (**1999**), 8(11), 2290-2303
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The partly folded states of .alpha.-lactalbumin (.alpha.-LA) exposed to acid soln. at pH 2.0 (A-state) or at neutral pH upon EDTA-mediated removal of the single **protein**-bound calcium ion (apo form) have been probed by limited proteolysis expts. These states are nowadays commonly considered to be molten globules and thus **protein**-folding intermediates. Pepsin was used for proteolysis at acid pH, while **proteinase** K and chymotrypsin at neutral pH. The expectations were that these proteolytic probes would detect sites and/or chain regions in the partly folded states of .alpha.-LA sufficiently dynamic, or even unfolded, capable of binding and adaptation to the specific stereochem. of the **protease**'s active site. A time-course anal. of the proteolytic events revealed that the fast, initial proteolytic cuts of the 123-residue chain of .alpha.-LA in its A-state or apo form by the three **proteases** occur at the same chain region 39-54, the actual site(s) of **cleavage** depending upon the **protease** employed. This region in native .alpha.-LA encompasses the .beta.-**sheets** of the **protein**. Subsequent **cleavages** occur mostly at chain regions 31-35 and 95-105. Four fragment species of .alpha.-LA have been isolated by reverse-phase high-performance liq. chromatog., and their conformational properties examd. by CD and **fluorescence** emission spectroscopy. The single chain fragment 53-103, contg. all the binding sites for calcium in native .alpha.-LA and cross-linked by two disulfide bridges, maintains in aq. buffer and in the presence of calcium ions a folded structure characterized by the same content of .alpha.-helix of the corresponding chain segment in native .alpha.-LA. Evidence for some structure was also obtained for the two-chain species 1-40 and 104-123, as well as 1-31 and 105-123, both systems being covalently linked by two disulfide bonds. In contrast, the **protein** species given by fragment 1-34 connected to fragment 54-123 or 57-123 via four disulfide bridges adopts in soln. a folded structure with the helical content expected for a native-like conformation. Of interest, the proteolytic fragment species herewith isolated correspond to the structural domains and subdomains of .alpha.-LA that can be identified by computational anal. of the three-dimensional structure of native .alpha.-LA. The fast, initial **cleavages** at the level of the .beta.-**sheet** region of native .alpha.-LA indicate that this region is highly mobile or even unfolded in the .alpha.-LA molten globule(s), while the rest of the **protein** chain maintains sufficient structure and rigidity to prevent extensive proteolysis. The subsequent **cleavages** at chain segment 95-105 indicate that also this region is somewhat mobile in the A-state or apo form of the **protein**. It is concluded that the overall domain topol. of native .alpha.-LA is maintained in acid or at neutral pH upon calcium depletion. Moreover, the mol. properties of the partly folded states of .alpha.-LA deduced here from proteolysis expts. do correlate with those derived from previous NMR and other physicochem. measurements.
REFERENCE COUNT: 87
REFERENCE(S): (1) Alexandrescu, A; Biochemistry 1993, V32, P1707 HCAPLUS
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(4) Chakrabartty, A; Biochemistry 1993, V32, P5560 HCAPLUS

(5) Chen, Y; Biochemistry 1974, V13, P3350 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:233995 HCAPLUS
DOCUMENT NUMBER: 130:277651
TITLE: Production of anticalins, recombinant antibody-like proteins with selected ligand affinity
INVENTOR(S): Skerra, Arne; Beste, Gerald; Schmidt, Frank; Stibora, Thomas
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9916873	A1	19990408	WO 1998-DE2898	19980925	<--
W: AU, CA, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
DE 19742706	A1	19990415	DE 1997-19742706	19970926	<--
AU 9911437	A1	19990423	AU 1999-11437	19980925	
EP 1017814	A1	20000712	EP 1998-954239	19980925	
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL, SE, FI					

PRIORITY APPLN. INFO.: DE 1997-19742706 A 19970926
WO 1998-DE2898 W 19980925

AB The invention concerns the prodn. of antibody-like anticalin **proteins** that are genetically mutated in order to bind selected ligands. For example, the bilin-binding **protein** (BBP) from Pieris brassicae and the human retinol-binding **protein** and apolipoprotein D can be mutated in their .beta.-**sheet loops**. The DNA of the selected ligand binding lipocalin mutant is fused to the gene coding for capsid **protein** pIII of the M13 filamentous bacteriophage. The fusion **protein** is expressed in bacteria or eukaryotic cells. The anticalins contain also coded **cleavage** sites for **proteinases**. Ligands that can bind to the anticalins are hapten type mols. or hapten conjugates. The fusion **protein** can be immobilized onto a solid surface; after ligand binding, the ligand or part of it can be sepd. A DNA library for lipocalin mutants of the BBP was constructed in a two step PCR procedure using synthetic primers and pBBP20-plasmid. The DNA fragments were cloned; after a series of procedures, phagemids were enriched in mutants that specifically bind to selected ligands. Glutaryl-4-aminofluorescein was conjugated with BSA and immobilized onto immuno sticks; the sticks were used for the repeated affinity enrichment of the phagemids. Selected phagemids were subcloned and expressed in E.coli; sequencing of the BBP gene cassette referred to four different gene products, named FluA, FluB, FluC, and FluD. The **proteins** were expressed in 50 mL and 5 L E.coli fermns.; **proteins** were affinity isolated using the fused Strap-Tag II. The ligand-binding properties of the anticalins were tested in ELISA; glutaryl-4-aminofluorescein-BSA conjugate was immobilized onto the plates; **protein** solns. were brought in contact with the ligand; after washing, the anticalin-ligand complex was incubated with streptavidin-alk. phosphatase. The enzyme conjugate recognized the Strap-Tag II; to detect bound **fluorescein**, the alk. phosphate hydrolyzed p-nitorphenyl phosphate was detected at 405 nm. The order of ligand binding was FluC > FluB > FluA; FluD and BBP did not bind to the ligand. **Fluorescence** titrn. was used to quantify the dissocn. consts. of FluA, FluB, and FluC with **fluorescein**, 4-aminofluorescein and glutaryl-4-aminofluorescein. Similarly, an antibody-like anticalin fusion peptide to Hepatitis C peptide epitope was produced and used in a sandwich ELISA.

REFERENCE COUNT: 8
REFERENCE(S): (1) Flower, D; BIOCHEMICAL JOURNAL 1996, V318, P1

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(3) Mueller, H; BIOCHEMISTRY 1994, V33(47), P14126 HCAPLUS
(5) Schmidt, F; EUROPEAN JOURNAL OF BIOCHEMISTRY 1994, V219(3), P855 HCAPLUS
(7) Sundaram, M; BIOCHEMICAL JOURNAL 1998, V334(1), P155 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:200809 HCAPLUS
DOCUMENT NUMBER: 124:254456
TITLE: Conformational changes in subdomain I of actin induced by proteolytic cleavage within the DNase I-binding loop. Energy transfer from tryptophan to AEDANS
AUTHOR(S): Kuznetsova, Irina; Antropova, Olga; Turoverov, Konstantin; Khaitlina, Sofia
CORPORATE SOURCE: Institute of Cytology, Russian Academy of Sciences, Tikhoretsky av., 4, St. Petersburg, 194064, Russia
SOURCE: FEBS Lett. (**1996**), 383(1,2), 105-8
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alteration of the actin **polypeptide** chain within the DNase I-binding **loop** by **cleavage** with E. coli A2 **protease** or subtilisin was shown to increase the efficiency of energy transfer from tryptophan residues to AEDANS attached to Cys-374. Anal. of structural and **fluorescence** data suggested that only two of four actin tryptophan residues, namely, Trp-340 and/or Trp-356, can be energy transfer donors. It was also found that labeling with AEDANS induces perturbations in the environment of the tryptophan residues, these perturbations being smaller in the **cleaved** actin. These changes are consistent with a shift of the C-terminal segment of actin monomer upon **cleavage** and confirm the existence of high conformational coupling between subdomains 1 and 2 of actin monomer. The authors also suggest that tryptophan residues 340 and/or 356 are located in the focus of this coupling.

L4 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:787462 HCAPLUS
DOCUMENT NUMBER: 123:221667
TITLE: Tryptophans 231 and 234 in Protein C Report the Ca2+-Dependent Conformational Change Required for Activation by the Thrombin-Thrombomodulin Complex
AUTHOR(S): Rezaie, Alireza R.; Esmon, Charles T.
CORPORATE SOURCE: Health Sciences Center, University of Oklahoma, Oklahoma, OK, 73104, USA
SOURCE: Biochemistry (**1995**), 34(38), 12221-6
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human **protein** C circulates as both single- and two-chain zymogens. Activation by the physiol. activation complex, thrombin-thrombomodulin, generates the anticoagulant enzyme, activated **protein** C. Ca2+ binding to the **protease** domain of **protein** C is accompanied by 5.5% quenching of intrinsic **fluorescence** that correlates with the conformational change required for the rapid activation by the thrombin-thrombomodulin complex. To map which Trp residues report this Ca2+ binding, candidate Trp residues at positions 84, 115, 145, 205, 231, and 234 were changed individually to Phe within a **protein** C deletion mutant lacking the Gla domain (GDPC). Of these, the Trp to Phe mutation at position 231 (W231F) eliminated the Ca2+-induced **fluorescence** quenching, and the Trp 234 to Phe mutation (W234F) increased the max. quenching in **protein** C to 9.4%. Upon Ca2+ binding, the **fluorescence** emission intensity of the W231F mutant was increased 3.4%. The Kd for this site (84 .mu.M) was similar to that of GDPC (Kd = 39 .mu.M). To

compare the properties of single- and two-chain **protein** C, we replaced the Lys156-Arg157 dipeptide **cleavage** site in **protein** C with Thr and Gln to form GDPCKR/TQ. GDPCKR/TQ and the two-chain form of **protein** C were activated at the same rate with the thrombin-thrombomodulin complex, they exhibited similar Ca2+ dependence for both activation and **fluorescence** quenching, and these enzymes had the same chromogenic activity. In contrast to the zymogen form, activated human Gla-domainless **protein** C did not undergo a Ca2+-induced **fluorescence** change. These results indicate that the environment of Trp 231 and 234 within the Ca2+ binding **loop** of the **protein** C zymogen are perturbed by Ca2+ binding to the zymogen.

L4 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:417899 HCAPLUS
DOCUMENT NUMBER: 123:26893
TITLE: Structure of the human gene encoding sterol regulatory element binding protein-1 (SREBF1) and localization of SREBF1 and SREB2 to chromosomes 17p11.2 and 22q13
AUTHOR(S): Hua, Xianxin; Wu, Jian; Goldstein, Joseph L.; Brown, Michael S.; Hobbs, Helen H.
CORPORATE SOURCE: Dep. Mol. Genetics, University Texas Southwestern Medical Center, Dallas, TX, 75235, USA
SOURCE: Genomics (**1995**), 25(3), 667-73
CODEN: GNMCEP; ISSN: 0888-7543
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sterol regulatory element binding **protein**-1 (SREBP1) and SREBP2 are structurally related **proteins** that control cholesterol homeostasis by stimulating transcription of sterol-regulated genes, including those encoding the low-d. lipoprotein (LDL) receptor and 3-hydroxy-3-methylglutaryl CoA synthase. SREBP1 and SREBP2 and 47% identical, and they share a novel structure comprising a transcriptionally active NH2-terminal basic helix-**loop**-helix-leucine zipper (bHLH-Zip) domain followed by a membrane attachment domain. **Cleavage** by a sterol-regulated **protease** frees the bHLH-Zip domain from the membrane and allows it to enter the nucleus. SREBP1 exists in several forms, possibly as a result of alternative splicing at both the 5' and the 3' ends of the mRNA. The genes for SREBP1 and SREBP2 have not been studied. In this paper we describe the cloning and characterization of the human SREBF1 gene. The gene is 26 kb in length and has 22 exons and 20 introns. The 5' and 3' sequences that differ between the two SREBP1 cDNAs are encoded by discrete exons, confirming the hypothesis that they result from alternative splicing. The chromosomal locations of human SREBF1 and SREBF2 were detd. by anal. of human-rodent somatic cell hybrids and **fluorescence** in situ hybridization. The SREBF1 gene mapped to the proximal short arm of chromosome 17 (17p11.2), and the SREBF2 gene was localized to the long arm of chromosome 22 (22q13).

L4 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:281884 HCAPLUS
DOCUMENT NUMBER: 122:75034
TITLE: Testing a model of the extracellular domain human tissue [factor] consistent with Fourier transform infrared spectroscopy
AUTHOR(S): Ross, J. B. A.; Hasselbacher, C. A.; Kumosinski, Thomas F.; King, Gregory; Laue, T. M.; Guha, A.; Nemerson, Y.; Konigsberg, W. H.; Rusinova, E.; Waxman, E.
CORPORATE SOURCE: Dep. Biochem., Mount Sinai Sch. Med., New York, NY, 10029, USA
SOURCE: ACS Symp. Ser. (**1994**), 576(Molecular Modeling), 113-22, 1 plate
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tissue factor (TF) is a membrane-anchored cell-surface **protein** that in complex with the serine **protease** Factor VIIa initiates

blood coagulation upon tissue damage. The authors have cloned and expressed the sol., cytoplasmic domain of TF (residues 1-218) (sTF) for anal. of structure and function. Global secondary structural elements were detd. using FTIR spectroscopy. The amide I band assignments indicated .apprx.15% .alpha.-helix, 23% extended strands, the remainder being turns, **loops**, .beta.-**sheet**, and 'other' structure. Secondary structure prediction algorithms using a knowledge-based approach that was constrained to the FTIR-detd. structural elements were used to generate a working model of sTF, which was energy minimized and generate a working model of sTF, which was energy minimized and equilibrated at 300 K using a Kollman force field. The predictions of this model were tested by anal. ultracentrifugation, proteolytic **cleavage**, and absorption and **fluorescence** spectra of Trp .fwdarw. Tyr and Trp .fwdarw. Phe mutants of sTF.

L4 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:429728 HCAPLUS
DOCUMENT NUMBER: 121:29728
TITLE: Generation of a Family of Protein Fragments for Structure-Folding Studies. 1. Folding Complementation of Two Fragments of Chymotrypsin Inhibitor-2 Formed by Cleavage at Its Unique Methionine Residue
AUTHOR(S): Prat Gay, G. de; Fersht, Alan R.
CORPORATE SOURCE: Department of Chemistry, Cambridge University, Cambridge, CB2 1EW, UK
SOURCE: Biochemistry (**1994**), 33(25), 7957-63
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The suitability of the barley chymotrypsin inhibitor-2 for study by fragmentation and complementation has been analyzed. The primary residue for binding to **proteases**, Met-59 (the unique methionine in the sequence), lies in a broad, solvent-exposed **loop**. The bond between Met-59 and Glu-60 was **cleaved** by cyanogen bromide. The two fragments thus obtained, i.e., CI-2(20-59) and CI-2(60-83), assoc. (KD = 42 nM) to yield a complex that has **fluorescence** and CD spectra identical to those of uncleaved chymotrypsin inhibitor-2. Recovery of native-like structure is further indicated by the ability of the complex to inhibit chymotrypsin, although the [I]50% is 140-fold higher than for the uncleaved inhibitor. CI-2(60-83) appears to be highly disordered in water, but fragment CI(20-59) forms a significant structure, as judged by its circular dichroism spectra and evidence from one-dimensional NMR. The CD spectra of CI-2(20-59) approach the baseline in 4 M guanidinium chloride but display characteristics of an .alpha.-helix in the presence of trifluoroethanol. Anal. ultracentrifugation shows no concn.-dependent change in the mol. wt. of the monomer of CI-2(20-59). Both one- and two-dimensional NMR of the complex [CI-2(20-59).cntdot.(60-83)] show unequivocally the presence of a folded structure, which appears to be slightly different from the uncleaved native **protein**.

L4 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:586177 HCAPLUS
DOCUMENT NUMBER: 109:186177
TITLE: Plasma serine proteinase inhibitors (serpins) exhibit major conformational changes and a large increase in conformational stability upon cleavage at their reactive sites
AUTHOR(S): Bruch, Marcel; Weiss, Verena; Engel, Juergen
CORPORATE SOURCE: Biocent., Univ. Basel, Basel, CH-4055, Switz.
SOURCE: J. Biol. Chem. (**1988**), 263(32), 16626-30
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intact and proteolytically-modified human serpins, .alpha.1-**proteinase** inhibitor, antithrombin III, .alpha.1-antichymotrypsin, and C1 inhibitor, were compared by CD, **fluorescence** spectroscopy, and resistance against unfolding by guanidine HCl. The modified **proteins** were prepd. from the intact and active inhibitors by selective proteolytic **cleavage** in their reactive

site **loops** and tested for complete loss of activity. Significant differences in the spectral properties between intact and modified inhibitors indicate that a major conformational rearrangement is triggered by the **cleavage**. This leads to a large increase in conformation stability as demonstrated by large shifts of the transition profiles recorded as a function of guanidine HCl concn. at 20.degree. by CD at 220 nm. Intact inhibitors were unfolded in 2 steps of about equal size centered at 0.8-1.7 and 2.5-3.5M denaturant, resp. Under identical conditions modified inhibitors are completely stable, and their denaturation occurs only well above 4M guanidine HCl in 1 or 2 steep transition steps. The similarity of the spectral changes and shifts in transition profiles for all 4 serpins studied indicate that the conformational changes and stabilization triggered by the modification hit are important common mechanistic features of this class of inhibitors. This is supported by the observation that ovalbumin, which is homologous with the serpins but apparently lacks inhibitory activity, exhibits neither spectral changes nor a significant change in stability upon proteolytic modification.

L4 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1983:14116 HCAPLUS
DOCUMENT NUMBER: 98:14116
TITLE: The effect of proteolytic enzymes on the infectivity of vaccinia virus
AUTHOR(S): Ichihashi, Yasuo; Tsuruhara, Takashi; Oie, Masayasu
CORPORATE SOURCE: Fac. Med., Niigata Univ., Asahi, 951, Japan
SOURCE: Virology (**1982**), 122(2), 279-89
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment of vaccinia virus strain IHD-J with proteolytic enzymes such as trypsin, chymotrypsin, thermolysin, pronase E, and papain did, whereas **protease** V8 did not, increase its infectivity. Virus treated with the enzymes at their optimal dose for activation were resistant to DNase; the membrane and core structures remained intact. **Proteins** assocd. with the viral membrane (VP110K, VP88K, VP54K, VP34K, VP32K, and VP14K) were digested at different rates which depended on the enzyme used, but **proteins** in the core region retained their mol. wt. The proteolytic activation of viral infectivity is related to a change in the virus surface **proteins**. To examine the viral **proteins** of enzyme-treated virus, the viral **proteins** were blotted onto nitrocellulose **sheets** after SDS-polyacrylamide gel electrophoresis, and stained with antisera and **fluorescein** isothiocyanate-labeled **Protein** A. The **proteins** specifically reactive with hyperimmune anti-IHD-J serum were VP43K and VP41K of intact virus, the 41-kilodalton (K) **cleavage** product in trypsin-treated virus, and the 43K and 36K **proteins** of papain-treated virus. Immune-staining profiles of virus treated with suboptimal enzyme doses showed that these **proteins** were derived from VP88K. The 30K **protein** detected in all enzyme-activated virus did not react with hyperimmune serum. Peptide anal. indicated that the 30K **protein** was a **cleavage** product of VP34K, and that confirmed that VP88K possessed the same peptides as VP43K. The findings suggest that the **cleavage** products derived from VP88K are the activated penetration factors for the 1st phase of uncoating.

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L6 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:378030 HCAPLUS
DOCUMENT NUMBER: 131:179425
TITLE: Inhibition of caspase activity does not prevent the signaling phase of apoptosis in prostate cancer cells
AUTHOR(S): Denmeade, Samuel R.; Lin, Xiaohui S.; Tombal, Bertrand; Isaacs, John T.
CORPORATE SOURCE: Johns Hopkins Oncology Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: Prostate (N. Y.) (**1999**), 39(4), 269-279
CODEN: PRSTDS; ISSN: 0270-4137
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB BACKGROUND. **Caspases** are a family of cysteine **proteases** capable of characteristically **cleaving** after an aspartic acid residue. Various members of the **caspase** family (e.g., **caspases** 8 and 9) have been implicated as crit. initiators in the signaling phase, while others (e.g., **caspases** 3, 6,and 7) have been implicated in the effector or execution phase of apoptosis. Thapsigargin (TG) is capable of inducing cell proliferation-independent apoptosis of prostate cancer cells. This study was undertaken to det. if **caspase** inhibition can prevent TG- or 5-fluorodeoxyuridine (5-FrdU)-induced apoptosis in prostate cancer cells. METHODS. **Caspase** activity was evaluated by Western blot anal. of the **cleavage** of retinoblastoma (Rb) **protein**, a **caspase** substrate during TG-induced death of prostate cancer cells. In addn., hydrolysis of **caspase**-specific **fluorescent** peptide substrates was assayed in lysates from TG-treated cells. Clonogenic survival assays were performed following treatment of rat AT3 and human TSU-Pr1 prostate cancer cell lines with TG and 5-FrdU in the presence and absence of peptide **caspase** inhibitors. AT3.1 cells transfected with the crmA gene, encoding a viral **protein** with **caspase**-inhibitory activity, were also tested for clonogenic survival following TG and 5-FrdU exposure. RESULTS. During treatment with TG, Rb is first dephosphorylated and then proteolytically **cleaved** into 100-kDa and 40-kDa forms, indicative of **caspase** activity. A 6-8-fold increase in class II (i.e., **caspases** 3, 7, and 10) hydrolysis of the **caspase** substrate Z-DEVD-AFC was obsd. after 24 h of TG or 5-FrdU. AT3 cells expressing crmA (i.e., an inhibitor of **caspases** 1, 4, and 8) were not protected from apoptosis induced by TG or 5-FrdU. The **caspase** inhibitors Z-DEVD-fmk (i.e., an inhibitor of **caspases** 3, 7, and 10) and Z-VAD-fmk (i.e., a general **caspase** inhibitor) were also unable to protect TSU and AT3 cells from apoptosis induced by TG or 5-FrdU. CONCLUSIONS. **Caspase** activation may play a role in the downstream effector phase of the apoptotic cascade; however, in this study, **caspase** inhibition did not prevent the signaling phase of apoptosis induced by two agents with distinct mechanisms of cytotoxicity, TG or 5-FrdU. These results suggest that **caspase** inhibition by recently described endogenous **caspase** inhibitors should not lead to development of resistance to TG. A strategy for targeting TG's unique cytotoxicity to metastatic prostate cancer cells is currently under development.
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(7) Cardone, M; Science 1998, V282, P1318 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:309578 HCAPLUS
DOCUMENT NUMBER: 131:100642
TITLE: Caspase-mediated cleavage of cytoskeletal actin plays

a positive role in the process of morphological apoptosis
AUTHOR(S): Mashima, Tetsuo; Naito, Mikihiko; Tsuruo, Takashi
CORPORATE SOURCE: Laboratory of Biomedical Research, Institute of Molecular and Cellular Biosciences, University of Tokyo, Tokyo, 113, Japan
SOURCE: Oncogene (**1999**), 18(15), 2423-2430
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tumors result from the imbalance between cell growth and apoptosis. One of the characteristic changes in cancers is the abnormality in cytoskeleton, which suggests some roles of cytoskeletal **proteins** in tumorigenesis or the maintenance of tumor cells. Previously the authors showed that cytoskeletal actin is the substrate of **caspases**, the **proteases** responsible for apoptosis, while the role of actin **cleavage** in apoptosis remained unknown. To examine the **cleavage** of actin in vivo, the authors extensively performed immunoblot anal. using actin fragment-specific antibody. Here, the authors showed that, in some solid tumor cells, induction of apoptosis was accompanied by **caspase**-dependent actin-**cleavage** to 15 and 31 kDa fragments in vivo. To elucidate the role of actin-**cleavage** further, the authors introduced actin **cleaved** -fragments. The authors found that ectopic expression of an actin 15 kDa fragment induces morphol. changes resembling those of apoptotic cells. The expression of the actin fragment induced a dramatic change of cellular actin localization, as visualized by enhanced green **fluorescent protein** (EGFP)-tagged actin, while the actin fragment expression did not cause **caspase** activation nor the **cleavage** of a marker substrate **protein**, poly (ADP-ribose) polymerase. These results indicate that actin **cleavage** could play a pos. role in the morphol. changes of apoptosis downstream of **caspase** activation.
REFERENCE COUNT: 46
REFERENCE(S): (1) Alnemri, E; Cell 1996, V87, P171 HCAPLUS
(2) Alnemri, E; J Cell Biochem 1997, V64, P33 HCAPLUS
(3) Asch, H; Cancer Res 1996, V56, P4841 HCAPLUS
(4) Brancolini, C; EMBO J 1995, V14, P5179 HCAPLUS
(5) Brancolini, C; J Cell Biol 1997, V139, P759 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:37963 HCAPLUS
DOCUMENT NUMBER: 130:164184
TITLE: Toxic bile salts induce rodent hepatocyte apoptosis via direct activation of Fas
AUTHOR(S): Faubion, William A.; Guicciardi, M. Eugenia; Miyoshi, Hideyuki; Bronk, Steven F.; Roberts, Patricia J.; Svingen, Phyllis A.; Kaufmann, Scott H.; Gores, Gregory J.
CORPORATE SOURCE: Division of Gastroenterology and Hepatology, Mayo Medical School, Clinic, and Foundation, Rochester, MN, 55905, USA
SOURCE: J. Clin. Invest. (**1999**), 103(1), 137-145
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cholestatic liver injury appears to result from the induction of hepatocyte apoptosis by toxic bile salts such as glycochenodeoxycholate (GCDC). Previous studies from this lab. indicate that cathepsin B is a downstream effector **protease** during the hepatocyte apoptotic process. Because **caspases** can initiate apoptosis, the present studies were undertaken to det. the role of **caspases** in cathepsin B activation. Immunoblotting of GCDC-treated McNtcp.24 hepatoma cells demonstrated **cleavage** of poly(ADP-ribose) polymerase and lamin B1 to fragments that indicate activation of effector

caspases. Transfection with CrmA, an inhibitor of **caspase** 8, prevented GCDC-induced cathepsin B activation and apoptosis. Consistent with these results, an increase in **caspase** 8-like activity was obsd. in GCDC-treated cells. Examn. of the mechanism of GCDC-induced **caspase** 8 activation revealed that dominant-neg. FADD inhibited apoptosis and that hepatocytes isolated from Fas-deficient lymphoproliferative mice were resistant to GCDC-induced apoptosis. After GCDC treatment, immunopptn. expts. demonstrated Fas oligomerization, and confocal microscopy demonstrated .DELTA.FADD-GFP (Fas-assocd. death domain-green **fluorescent protein**), aggregation in the absence of detectable Fas ligand mRNA. Collectively, these data suggest that GCDC-induced hepatocyte apoptosis involves ligand-independent oligomerization of Fas, recruitment of FADD, activation of **caspase** 8, and subsequent activation of effector **proteases**, including downstream **caspases** and cathepsin B.

REFERENCE COUNT: 42
REFERENCE(S):
(1) Adjei, P; J Clin Invest 1996, V98, P2588 HCAPLUS
(2) Ahmad, M; Cancer Res 1997, V57, P615 HCAPLUS
(3) Alnemri, E; Cell 1996, V87, P171 HCAPLUS
(4) Aragane, Y; J Cell Biol 1998, V140, P171 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:766905 HCAPLUS
DOCUMENT NUMBER: 130:137744
TITLE: Hypoxia induces apoptosis in human neuroblastoma SK-N-MC cells by caspase activation accompanying cytochrome c release from mitochondria
AUTHOR(S): Araya, Runa; Uehara, Takashi; Nomura, Yasuyuki
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Department of Pharmacology, Hokkaido University, Sapporo, 060-0812, Japan
SOURCE: FEBS Lett. (**1998**), 439(1,2), 168-172
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have attempted to elucidate the mechanism of apoptotic cell death induced by hypoxia (very low oxygen conditions) in neuronal cells. Human neuroblastoma SK-N-MC cells under hypoxic conditions resulted in apoptosis in a time-dependent manner estd. by DNA fragmentation assay and nuclear morphol. stained with **fluorescent** chromatin dye. Pretreatment with Z-Asp-CH2-DCB, a **caspase** inhibitor, suppressed the DNA ladder in response to hypoxia in a concn.-dependent manner. An increase in **caspase**-3-like **protease** (DEVDase) activity was obsd. during apoptosis, but no **caspase**-1 activity (YVADase) was detected. To confirm the involvement of **caspase**-3 during apoptosis, Western blot anal. was performed using anti-**caspase**-3 antibody. The 20- and 17-kDa **proteins**, corresponding to the active products of **caspase**-3, were generated in hypoxia-challenged lysates in which processing of the full length form of **caspase**-3 was evident. With a time course similar to this **caspase**-3 activation, hypoxic stress caused the **cleavage** of PARP, yielding an 85-kDa fragment typical of **caspase** activity. In addn., **caspase**-2 was also activated by hypoxia, and the stress elicited the release of cytochrome c into the cytosol during apoptosis. These results suggest that **caspase** activation and cytochrome c release play roles in hypoxia-induced neuronal apoptosis.

REFERENCE COUNT: 34
REFERENCE(S):
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(2) Auer, R; Diabetes 1984, V33, P1090 HCAPLUS
(3) Auer, R; Stroke 1986, V17, P699 HCAPLUS
(5) Ferrer, I; Acta Neuropathol 1997, V94, P583 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:716682 HCAPLUS
DOCUMENT NUMBER: 130:104925
TITLE: Role of Caspases in Immunotoxin-Induced Apoptosis of Cancer Cells
AUTHOR(S): Keppler-Hafkemeyer, Andrea; Brinkmann, Ulrich; Pastan, Ira
CORPORATE SOURCE: Laboratory of Molecular Biology Division of Basic Sciences National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Biochemistry (**1998**), 37(48), 16934-16942
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunotoxins composed of antibodies linked to plant or bacterial toxins are being evaluated in the treatment of cancer. It is known that the toxin moieties of immunotoxins, including Pseudomonas exotoxin A (PE), diphtheria toxin, and ricin, are capable of inducing apoptosis. Since the efficiency of induction of apoptosis and the apoptosis pathway may have direct effects on the therapeutic usefulness of immunotoxins, we have studied how B3(Fv)-PE38, a genetically engineered immunotoxin in which the Fv fragment of an antibody is fused to a mutated form of PE, induces apoptosis of the MCF-7 breast cancer cell line. We show for the first time that a PE-contg. immunotoxin activates ICE/ced-3 **proteases**, now termed **caspases**, and causes characteristic **cleavage** of the "death substrate" poly(ADP)-ribose polymerase (PARP) to an 89 kDa fragment with a time course of **cleavage** comparable to that induced by TNF.alpha.. Also the **fluorescent** substrate, DEVD-AFC, is **cleaved** 2-4-fold more rapidly by lysates from B3(Fv)-PE38 treated MCF-7 cells than untreated control cells, suggesting that a CPP32-like **caspase** is involved in B3(Fv)-PE38-mediated apoptosis. B3(Fv)-PE38-induced PARP **cleavage** is inhibited by several **protease** inhibitors known to inhibit **caspases** (zVAD-fmk, zDEVD-fmk, zIETD-fmk) as well as by overexpression of Bcl-2 providing addnl. evidence for **caspase** involvement. ZVAD-fmk, a broad spectrum inhibitor of most mammalian **caspases**, prevents the early morphol. changes and loss of cell membrane integrity produced by B3(Fv)-PE38, but not its ability to inhibit **protein** synthesis, arrest cell growth, and subsequently kill cells. Despite inhibition of apoptosis, the immunotoxin is still capable of selective cell killing, which indicates that B3(Fv)-PE38 kills cells by two mechanisms: one requires **caspase** activation, and the other is due to the arrest of **protein** synthesis caused by inactivation of elongation factor 2. The fact that an immunotoxin can specifically kill tumor cells without the need of inducing apoptosis makes such agents esp. valuable for the treatment of cancers that are protected against apoptosis, e.g., by overexpression of Bcl-2.
REFERENCE COUNT: 51
REFERENCE(S): (1) Allam, M; Cancer Res 1997, V57, P2615 HCAPLUS
(2) Alnemri, E; Cell 1996, V87, P171 HCAPLUS
(3) Armstrong, R; J Biol Chem 1996, V271, P16850 HCAPLUS
(4) Beidler, D; J Biol Chem 1995, V270, P16526 HCAPLUS
(5) Boulakia, C; Oncogene 1996, V12, P529 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:638936 HCAPLUS
DOCUMENT NUMBER: 129:341895
TITLE: Prodomain-dependent nuclear localization of the caspase-2 (Nedd2) precursor. A novel function for a caspase prodomain
AUTHOR(S): Colussi, Paul A.; Harvey, Natasha L.; Kumar, Sharad
CORPORATE SOURCE: Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science, Adelaide, 5000, Australia
SOURCE: J. Biol. Chem. (**1998**), 273(38), 24535-24542
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Caspases** are cysteine **proteases** that play an essential role in apoptosis by **cleaving** several key cellular **proteins**. Despite their function in apoptosis, little is known about where in the cell they are localized and whether they are translocated to specific cellular compartments upon activation. In the present paper, using Aequorea victoria green **fluorescent protein** (GFP) fusion constructs, the authors detd. the localization of Nedd2 (mouse **caspase**-2) and showed that both precursor and processed **caspase**-2 localize to the cytoplasmic and the nuclear compartments of transfected NIH-3T3 cells. The authors demonstrated that the nuclear localization of **caspase**-2 was strictly dependent on the presence of the pro-domain. A **caspase**-2 pro-domain-GFP localized to dot- and fiber-like structures, mostly in the nucleus, whereas a **protein** lacking the pro-domain was largely concd. in the cytoplasm. It was also shown that an N-terminal fusion of the pro-domain of **caspase**-2 to **caspase**-3 mediated nuclear transport of **caspase**-3, which is normally localized in the cytoplasm. These results suggest that, in addn. to roles in dimerization and recruitment through adaptors, the **caspase**-2 pro-domain has a novel function in nuclear transport.

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:541778 HCAPLUS
DOCUMENT NUMBER: 129:243599
TITLE: Intracellular aggregate formation of dentatorubral-pallidoluysian atrophy (DRPLA) protein with the extended polyglutamine
AUTHOR(S): Miyashita, Toshiyuki; Nagao, Kazuaki; Ohmi, Kazuhiro; Yanagisawa, Hiroko; Okamura-Oho, Yuko; Yamada, Masao
CORPORATE SOURCE: Department of Genetics and Pathology, National Children's Medical Research Center, Tokyo, 154-8509, Japan
SOURCE: Biochem. Biophys. Res. Commun. (**1998**), 249(1), 96-102
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dentatorubral-pallidoluysian atrophy (DRPLA) is an autosomal dominant neurodegenerative disorder caused by the abnormal CAG triplet-repeat expansion resulting in an elongated polyglutamine (polyQ) stretch. We have recently showed that the DRPLA **protein** is **cleaved** during apoptosis by **caspase**-3, one of the cysteine **protease** family members known to be activated during apoptosis. We report here the subcellular localization of the DRPLA **protein** by fusing the green **fluorescent protein** as a tag. The full length DRPLA **protein** is localized predominantly but not exclusively in the nucleus regardless of the length of the polyQ stretch. In contrast, an N-terminal-deleted fragment contg. polyQ produced by the proteolytic **cleavage** with **caspase**-3 is found both in the nucleus and the cytoplasm. Moreover, the same fragment with the elongated polyQ showed aggregation when overexpressed. Some cells with aggregate formation showed apoptotic phenotype. These findings raise the possibility that the DRPLA **protein** processed by **caspase**-3 may lead to aggregation of the **protein** resulting in the development of neurodegeneration. (c) 1998 Academic Press.

L6 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:300008 HCAPLUS
DOCUMENT NUMBER: 129:90001
TITLE: Inhibition of epidermal growth factor receptor kinase induces protease-dependent apoptosis in human colon cancer cells
AUTHOR(S): Karnes, William E., Jr.; Weller, Shaun G.; Adjei, Philip N.; Kottke, Timothy J.; Glenn, Kahlil S.;

Gores, Gregory J.; Kaufmann, Scott H.
CORPORATE SOURCE: Division of Gastroenterology, Mayo Clinic, Rochester, MN, USA
SOURCE: Gastroenterology (**1998**), 114(5), 930-939
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The epidermal growth factor receptor (EGFR) is under investigation as a therapeutic target for cancers. Colon cancer cell lines are variably dependent on autocrine stimulation of EGFR. We therefore examd. the effects of a selective EGFR tyrosine kinase inhibitor, PD 153035, on proliferation and survival of five colon cancer cell lines whose autonomous proliferation is either EGFR ligand dependent or EGFR ligand independent. Effects of inhibitors were screened by MTS growth assays, [3H]thymidine incorporation, terminal deoxynucleotidyl transferase-medaited deoxyuridine triphosphate nick-end labeling assay, **fluorescence** microscopy, immunoblotting, and in vitro **protease** assays. PD 153035 caused dose-dependent cytostasis (200 nmol/L to 1 .mu.mol/L) and apoptosis (>10 .mu.mol/L) in ligand-dependent cell lines and caused variable apoptosis (>10 .mu.mol/L) but no cytostasis in ligand-independent cell lines. Apoptosis induced by 10 .mu.mol/L PD 153035 was not assocd. with induction of p53 **protein** expression but was accompanied by activation of **caspases** that **cleave** poly(ADP-ribose) polymerase, lamin B1, and Bcl-2. Inhibition of **caspase** 3-like **protease** activity by DEVD-fluoromethylketone significantly delayed the onset of PD 153035-induced apoptosis. The EGFR tyrosine kinase inhibitor PD 153035 induces cytostasis and **caspase**-dependent apoptosis in EGFR ligand-dependent colon cancer cell lines. These observations encourage further investigation of EGFR tyrosine kinase inhibitors for treatment of colorectal neoplasms.

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:272306 HCAPLUS
DOCUMENT NUMBER: 129:25240
TITLE: Detection of programmed cell death using fluorescence energy transfer
AUTHOR(S): Xu, Xiang; Gerard, Amy L. V.; Huang, Betty C. B.; Anderson, David C.; Payan, Donald G.; Luo, Ying
CORPORATE SOURCE: Rigel, Inc., Sunnyvale, CA, 94086, USA
SOURCE: Nucleic Acids Res. (**1998**), 26(8), 2034-2035
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Fluorescence** energy transfer (FRET) can be generated when green **fluorescent protein** (GFP) and blue **fluorescent protein** (BFP) are covalently linked together by a short peptide. **Cleavage** of this linkage by **protease** completely eliminates FRET effect. **Caspase**-3 (CPP32) is an important cellular **protease** activated during programmed cell death. An 18 amino acid peptide contg. CPP32 recognition sequence, DEVD, was used to link GFP and BFP together. CPP32 activation can be monitored by FRET assay during the apoptosis process.

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L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:272306 HCAPLUS
DOCUMENT NUMBER: 129:25240
TITLE: Detection of programmed cell death using fluorescence energy transfer
AUTHOR(S): Xu, Xiang; Gerard, Amy L. V.; Huang, Betty C. B.; Anderson, David C.; Payan, Donald G.; Luo, Ying
CORPORATE SOURCE: Rigel, Inc., Sunnyvale, CA, 94086, USA
SOURCE: Nucleic Acids Res. (**1998**), 26(8), 2034-2035
CODEN: NARHAD; ISSN: 0305-1048
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 9-5 (Biochemical Methods)
ABSTRACT:

Fluorescence energy transfer (FRET) can be generated when green ***fluorescent*** **protein** (GFP) and blue **fluorescent** ***protein*** (BFP) are covalently linked together by a short peptide. ***Cleavage*** of this linkage by **protease** completely eliminates FRET effect. **Caspase**-3 (CPP32) is an important cellular ***protease*** activated during programmed cell death. An 18 amino acid peptide contg. CPP32 recognition sequence, DEVD, was used to link GFP and BFP together. CPP32 activation can be monitored by FRET assay during the apoptosis process.

SUPPL. TERM: programmed cell death fluorescence energy transfer
INDEX TERM: Proteins (specific proteins and subclasses)
ROLE: NUU (Nonbiological use, unclassified); USES (Uses)
(Blue fluorescent protein; detection of programmed cell death using fluorescence energy transfer)
INDEX TERM: Fluorometry
(Fluorescence energy transfer; detection of programmed cell death using fluorescence energy transfer)
INDEX TERM: Apoptosis
Energy transfer
(detection of programmed cell death using fluorescence energy transfer)
INDEX TERM: Green fluorescent protein
ROLE: NUU (Nonbiological use, unclassified); USES (Uses)
(detection of programmed cell death using fluorescence energy transfer)
INDEX TERM: 9001-92-7, Protease 169592-56-7, Caspase-3
ROLE: NUU (Nonbiological use, unclassified); USES (Uses)
(detection of programmed cell death using fluorescence energy transfer)

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(FILE 'HOME' ENTERED AT 15:57:17 ON 19 OCT 2001)

FILE 'CROPU, DGENE, DPCI, ENCOMPPAT, ENCOMPPAT2, EUROPATFULL, HCAOLD, HCAPLUS, IFIPAT, INPADOC, JAPIO, PAPERCHEM2, PATDD, PATDPA, PATOSDE, PATOSEP, PATOSWO, PCTFULL, PIRA, RAPRA, SYNTHLINE, TULSA, TULSA2, USPATFULL, WPIDS' ENTERED AT 16:04:12 ON 19 OCT 2001

L1 121678 S (PROTEIN OR POLYPEPTIDE) (L) FLUORES?
L2 17030 S L1 (L) (PROTEASE OR PROTEINASE) (L) CLEAV?
L3 7433 S L2 (L) (LOOP OR SHEET)
L4 251 S L3 (L) CASPASE
L5 251 DUP REM L4 (0 DUPLICATES REMOVED)
L6 66 S L5 AND PY<=1999
L7 66 S L6 AND ASSAY
L8 21 S L7 AND (GREEN FLUORESCENT PROTEIN OR BLUE FLUORESCENT PROTE

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L8 ANSWER 1 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999066324 PCTFULL
TITLE (ENGLISH): A BIOLUMINESCENCE RESONANCE ENERGY TRANSFER (BRET) SYSTEM AND ITS USE
TITLE (FRENCH): SYSTEME DE TRANSFERT D'ENERGIE DE RESONANCE PAR BIOLUMINESCENCE ET UTILISATION DUDIT SYSTEME
INVENTOR(S): JOLY, Erik; JOHNSON, Carl, H.; PISTON, David, W.
PATENT ASSIGNEE(S): JOLY, Erik; JOHNSON, Carl, H.; PISTON, David, W.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9966324	**A2**	**19991223**

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-CA561 19990616
PRIORITY (ORIGINAL): US 1998-60/089623 19980616

ABEN This invention provides bioluminescence resonance energy transfer (BRET) system that comprises four parts: 1) a bioluminescent **protein** that has luciferase activity; 2) an acceptor fluorophore that can accept the energy from the bioluminescent **protein** when they are associated, in the presence of the appropriate substrate; 3) a modulator that influences the proximity or the orientation of the bioluminescent **protein** and the fluorophore, and 4) an appropriate substrate to activate the luciferase activity of the bioluminescent **protein**. The components of this system interact to influence the spatial relationship between the bioluminescent **protein** and the fluorophore, that is demonstrated by the light emission from the system. The modulator can be a single entity, covalently attached to both the bioluminescent **protein** and the fluorophore, it can be two separate entities, each linked covalently to either the bioluminescent **protein** or the fluorophore, or an alternative configuration that falls within the scope of the invention. Thissystem can be used in both in vivo or in vitro **assays** to detect molecular changes in a wide variety of applications, and is amenable to automation. In particular, it is useful for assaying **protein** interactions, enzyme activities and the concentration of analytes or signaling molecules in cells or in solution.

ABFR L'invention concerne un syst me de transfert d' nergie de r sonance par bioluminescence (BRET) constitu de quatre parties: 1) une prot ine bioluminescente ayant une activit lucif rase; 2) un fluorophore accepteur pouvant accepter l' nergie manant de la prot ine bioluminescente lorsqu'ils sont associ s, en pr sence du substrat appropri ; 3) un modulateur qui influence la proximit ou l'orientation de la prot ine bioluminescente et du fluorophore; et 4) un substrat appropri pour d clencher l'activit lucif rase de la prot ine bioluminescente. Les composants de ce syst me interagissent pour influencer la relation spatiale entre la prot ine bioluminescente et le fluorophore, ce que fait appara tre l' mission de lumi re provenant du

syst me. Le modulateur peut tre une seule entit fix e de mani re covalente la fois la prot ine bioluminescente et au fluorophore; il peut aussi tre deux entit s distinctes li es chacune de mani re covalente soit la prot ine bioluminescente soit au fluorophore; il peut enfin pr senter une configuration substitutive ressortissant au domaine de l'invention. Ce syst me peut tre utilis dans des dosages in vivo ou in vitro pour d tecter des modifications mol culaires dans de nombreuses applications, et se pr te l'automatisation. Le syst me convient en particulier pour analyser des interactions prot iques, des activit s enzymatiques ou la concentration de substances analyser ou de mol cules marqueurs dans des cellules ou dans une solution.

L8 ANSWER 2 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999058663 PCTFULL
TITLE (ENGLISH): METHODS AND COMPOSITIONS FOR SCREENING FOR MODULATORS OF IgE
SYNTHESIS, SECRETION AND SWITCH REARRANGEMENT
TITLE (FRENCH): PROCEDES ET COMPOSITIONS SERVANT AU CRIBLAGE DE MODULATEURS DE
SYNTHESE, DE SECRETION ET DE REMANIEMENT DE COMMUTATION DE CLASSE POUR
L'IgE
INVENTOR(S): FERRICK, David, A.; SWIFT, Susan, E.; ARMSTRONG, Randall; FOX, Bryan
PATENT ASSIGNEE(S): RIGEL PHARMACEUTICALS, INC.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9958663	**A1**	**19991118**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
APPLICATION INFO.: WO 1999-US10497 19990512
PRIORITY (ORIGINAL): US 1998-09/076624 19980512
ABEN The invention relates to methods and compositions useful in screening for modulators of IgE synthesis, secretion and switch rearrangement.
ABFR L'invention concerne des proc d s et des compositions servant au criblage de modulateurs de synth se, de s cr tion et de remaniement de commutation de classe pour l'IgE.

L8 ANSWER 3 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999057535 PCTFULL
TITLE (ENGLISH): RECOMBINANT CELL LINE AND SCREENING METHOD FOR IDENTIFYING AGENTS
WHICH REGULATE APOPTOSIS AND TUMOR SUPPRESSION
TITLE (FRENCH): LIGNEE CELLULAIRE RECOMBINANTE ET PROCEDE DE CRIBLAGE POUR
IDENTIFIER DES AGENTS REGULANT L'APOPTOSE ET LA SUPPRESSION D'UNE TUMEUR
INVENTOR(S): WHITE, Eileen; THOMAS, Anju; KASOF, Gary; GOYAL, Lakshmi
PATENT ASSIGNEE(S): RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9957535	**A2**	**19991111**

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK

EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL
PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ
MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU
MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD
TG

APPLICATION INFO.: WO 1999-US9793 19990506
PRIORITY (ORIGINAL): US 1998-60/084664 19980507
US 1998- 19980701
US 1998-60/091391 19980715
US 1998- 19981109

ABEN This invention provides recombinant cell lines and screening methods useful for identifying agents that induce apoptosis in target cells and therefore may be used to advantage in the treatment of neoplastic disorders.

ABFR L'invention concerne des lignees cellulaires recombinantes et des procedes de criblage qui permettent d'identifier des agents regulant l'apoptose dans des cellules cibles, et peuvent donc etre utilises utilement dans le traitement de maladies cancereuses.

L8 ANSWER 4 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999047963 PCTFULL
TITLE (ENGLISH): CONFOCAL MICROSCOPY IMAGING SYSTEM
TITLE (FRENCH): SYSTEME D'IMAGERIE CONFOCAL POUR MICROSCOPIE
INVENTOR(S): TRAUTMAN, Jay, K.; HARRIS, Timothy, D.; HANSEN, Richard, L.; KARSH, William; NICKLAUS, Neal, A.
PATENT ASSIGNEE(S): PRAELUX INCORPORATED
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9947963	**A1**	**19990923**

DESIGNATED STATES: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL
PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ
MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU
MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD
TG

APPLICATION INFO.: WO 1999-US5589 19990316
PRIORITY (ORIGINAL): US 1998-09/042527 19980316

ABEN A confocal imaging system utilizing an elongated beam. Specific embodiments are directed to the apparatus with charged couple devices (CCD) and those in which the apparatus is used in **fluorescent** object observation.

ABFR La presente invention concerne un systeme d'imagerie confocal utilisant un faisceau allonge. Les modes de realisations specifiques de cette invention concernent un appareil a dispositifs de couplage de charge (CCD) et ceux dans lequel l'appareil est utilise pour une observation d'un objet **fluorescent**.

L8 ANSWER 5 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999036536 PCTFULL
TITLE (ENGLISH): METHODS AND COMPOSITIONS TO ALTER TISSUE SUSCEPTIBILITY TO IMMUNE INJURY, TO PROGRAMMED CELL DEATH, AND TO CLEARANCE BY THE RETICULOENDOTHELIAL SYSTEM
TITLE (FRENCH): METHODES ET COMPOSITIONS PERMETTANT DE MODIFIER LA SENSIBILITE DES TISSUS FACE AUX LESIONS IMMUNITAIRES, A LA MORT CELLULAIRE PROGRAMMEE ET A LA CLAIRANCE PAR LE SYSTEME RETICULO-ENDOTHELIAL

INVENTOR(S): SIMS, Peter, J.; WIEDMER, Therese; ZHAO, Ji
PATENT ASSIGNEE(S): BLOOD CENTER RESEARCH FOUNDATION
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9936536	**A2**	**19990722**

DESIGNATED STATES: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1999-US1087 19990119
PRIORITY (ORIGINAL): US 1998-60/071950 19980120

ABEN A method for extending the viability of mammalian cells or tissues comprising the step of inhibiting the expression of native PL scramblase within the cell or tissue is disclosed. In another embodiment of the invention, a method of decreasing the viability, metastatic or invasive potential of cancer cells, cancerous tissue, or viral-infected cell by causing increased expression or activity of PL scramblase **protein** within the cell or tissue is disclosed.

ABFR La presente invention concerne une methode d'accroissement de la viabilite des cellules ou des tissus mammiferes, consistant a inhiber l'expression de la PL-scramblase native dans les cellules ou les tissus. Dans un autre mode de realisation, l'invention concerne une methode de reduction du potentiel metastatique et invasif ainsi que du potentiel de viabilite des cellules cancereuses, des tissus cancereux, ou des cellules infectees par virus, par l'augmentation de l'expression ou l'activite de la proteine PL-scramblase dans les cellules ou les tissus en question.

L8 ANSWER 6 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999019352 PCTFULL
TITLE (ENGLISH): METHODS AND COMPOSITIONS TO ALTER THE CELL SURFACE EXPRESSION OF PHOSPHATIDYLSERINE AND OTHER CLOT-PROMOTING PLASMA MEMBRANE PHOSPHOLIPIDS
TITLE (FRENCH): METHODES ET COMPOSITIONS PERMETTANT DE MODIFIER L'EXPRESSION DE LA SURFACE CELLULAIRE DE LA PHOSPHATIDYLSERINE ET D'AUTRES PHOSPHOLIPIDES DE MEMBRANE PLASMIQUE FAVORISANT LA FORMATION DE CAILLOTS
INVENTOR(S): WIEDMER, Therese; SIMS, Peter, J.
PATENT ASSIGNEE(S): BLOOD CENTER RESEARCH FOUNDATION
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9919352	**A2**	**19990422**

DESIGNATED STATES: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US20535 19981001
PRIORITY (ORIGINAL): US 1997-08/949246 19971010

ABEN A **protein** preparation that mediates Ca⁺² transbilayer movement of phospholipid is disclosed. Additionally, a modified or mutated **protein** preparation, wherein the **protein** has a reduced ability to mediate transbilayer movement, is disclosed. In a preferred form of the invention, the **protein** has been modified such that post-translational modification can no longer occur.

ABFR L'invention concerne une preparation de proteines induisant le transport du Ca²⁺ a travers la double couche de phospholipides. En outre, l'invention concerne une preparation de proteines modifiees ou mutantes, dans laquelle la proteine presente une capacite reduite a induire le transport a travers une double couche.

Dans une mode de realisation prefere de l'invention, la proteine a ete modifiee de telle maniere, qu'une modification apres traduction ne peut plus avoir lieu.

L8 ANSWER 7 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999016875 PCTFULL
TITLE (ENGLISH): A METHOD FOR SELECTIVELY CONTROLLING MEMBRANE **PROTEIN** DISPLAY AND **PROTEIN** SECRETION IN EUKARYOTIC CELLS
TITLE (FRENCH): PROCEDE SERVANT A EFFECTUER LE CONTROLE SELECTIF DE LA PRESENCE D'UNE PROTEINE DE MEMBRANE ET DE LA SECRETION DE PROTEINES DANS DES CELLULES EUCARYOTES
INVENTOR(S): MORROW, Jon, S.; DEVARAJAN, Prasad
PATENT ASSIGNEE(S): YALE UNIVERSITY
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9916875	**A1**	**19990408**

DESIGNATED STATES: AU CA JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US20364 19980930
PRIORITY (ORIGINAL): US 1997-60/060559 19970930

ABEN A method and related compositions are disclosed that modulate the presence on a cell surface membrane of selected integral membrane **proteins**, or modulate the secretion of selected secretory **proteins**, by increasing or decreasing the intracellular transport of the **protein** form the endoplasmic reticulum to and through the cis-Golgi apparatus. Associated methods are disclosed to identify whether the intracellular transport of a specific **protein** is mediated by the spectrin-ankyrin-adapter **protein** trafficking system (SAATS). Related methods to determine whether a candidate compound inhibits or enhances the intracellular transport of a selected **protein** from the endoplasmic reticulum to the cis-Golgi apparatus by SAATS also are disclosed. Disclosed agents and methods are applicable for a variety of uses, including as immunoregulators, ion transport inhibitors, vascular modulators and cancer chemotherapeutics.

ABFR Procede et compositions correspondantes modulant la presence sur une membrane de surface cellulaire de proteines de membrane entieres selectionnees ou la secretion de proteines secretrices selectionnees, ce qui consiste a augmenter ou a diminuer le transport intracellulaire de la proteine depuis le reticulum endoplasmique vers et a travers l'appareil de cis-Golgi. Des procedes associes permettent d'identifier si le transport intracellulaire d'une proteine specifique a pour mediateur le systeme de trafic de proteines d'adaptation de spectrine et ankyrine (SAATS). Des procedes correspondants servent a determiner si un compose candidat inhibe ou augmente le transport intracellulaire d'une proteine selectionnee depuis le reticulum endoplasmique vers l'appareil de cis-Golgi par SAATS. Des agents et des procedes peuvent etre mis en application dans une variete de domaines, y compris en tant qu'immunoregulateurs, inhibiteurs de transport d'ions, modulateurs vasculaires et agents chimiotherapeutiques contre le cancer.

L8 ANSWER 8 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1999011801 PCTFULL
TITLE (ENGLISH): **PROTEASE** BASED GENE SWITCHING SYSTEM
TITLE (FRENCH): SYSTEMES DE COMMUTATION DE GENES A BASE DE **PROTEASES**
INVENTOR(S): BROAD, Peter, Michael; CHARLES, Andrew, David; HOLLIS, Melvyn; MacCALLUM, Linda, Jean; SCANLON, David, John

PATENT ASSIGNEE(S): ZENECA LIMITED
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9911801	**A2**	**19990311**

DESIGNATED STATES: CA IL JP US AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-GB2596 19980828
PRIORITY (ORIGINAL): GB 1997-9718591.2 19970903

ABEN The present invention relates to materials and methods for **protease**-based gene switching systems, wherein a transcription factor is bound to a membrane via **protease cleavage** site. It also relates to the use of such materials and methods in the identification of substrates and inhibitors of **proteases** and in the design of altered specificity **proteases**.

ABFR La pr sente invention concerne des mati res et des m thodes destin es des syst mes de commutation de g nes base de prot ase, un facteur de transcription tant li une membrane via un site de clivage de prot ase. L'invention concerne galement l'utilisation de ces mati res et m thodes dans l'identification de substrats et d'inhibiteurs de prot ases et dans la conception de prot ases sp cificit alt r e.

L8 ANSWER 9 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998056892 PCTFULL
TITLE (ENGLISH): HUMAN TUMOR NECROSIS FACTOR RECEPTOR TR9
TITLE (FRENCH): RECEPTEUR HUMAIN TR9 DU FACTEUR DE NECROSE TUMORALE
INVENTOR(S): NI, Jian; YU, Guo-Liang; FAN, Ping; GENTZ, Reiner, L.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9856892	**A1**	**19981217**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1998-US11932 19980610
PRIORITY (ORIGINAL): US 1997-60/052991 19970611

ABEN The present invention relates to a novel member of the tumor necrosis factor family of receptors. In particular, isolated nucleic acid molecules are provided encoding the human TR9 receptor. TR9 **polypeptides** are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of TR9 receptor activity.

ABFR La presente invention concerne un nouveau membre de la famille des recepteurs du facteur de necrose tumorale. Elle concerne en particulier des molecules d'acide nucleique codant le recepteur humain TR9. Elle concerne en outre des **polypeptides** TR9 ainsi que des vecteurs, des cellules hotes, et des methodes recombinantes permettant de produire lesdits **polypeptides**. L'invention concerne enfin des methodes de selection permettant d'identifier des agonistes et des antagonistes de l'activite du recepteur TR9.

L8 ANSWER 10 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent

ACCESSION NUMBER: 1998054205 PCTFULL
TITLE (ENGLISH): SELECTIVE INDUCTION OF CELL DEATH BY DELIVERY OF AMINO-TERMINAL INTERLEUKIN-1-ALPHA PRO-PIECE **POLYPEPTIDE**
TITLE (FRENCH): INDUCTION SELECTIVE DE LA MORT CELLULAIRE PAR ADMINISTRATION D'UN **POLYPEPTIDE** DE MOITIE DE TERMINAISON N AMINO D'INTERLEUKINE-1-ALPHA
INVENTOR(S): POLLOCK, Allan, S.; LOVETT, David, H.; TURCK, Johanna
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9854205	**A1**	**19981203**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-US10839	19980528
PRIORITY (ORIGINAL):	US 1997-60/048137	19970530
	US 1998-09/065647	19980527

ABEN The present invention is directed to compositions and methods for selective induction of apoptosis in cancer cells, particularly malignant cancer cells, by delivery of an IL-1#agr# propiece **polypeptide** (e.g., a native IL-1#agr# propiece **polypeptide**, including IL-1#agr# propiece **polypeptide** variant) to a cancer cell.

ABFR L'invention concerne des compositions et des procedes servant a effectuer l'induction selective de l'apoptose dans des cellules cancereuses, en particulier, des cellules malignes, par administration d'un **polypeptide** de moitie de terminaison N IL-1#agr# (par exemple, un **polypeptide** natif de moitie de terminaison N IL-1#agr#, y compris une variante de ce dernier) a une cellule cancereuse.

L8 ANSWER 11 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998053091 PCTFULL
TITLE (ENGLISH): SCREENING **ASSAYS** FOR AGENTS THAT ALTER INHIBITOR OF APOPTOSIS (IAP) **PROTEIN** REGULATION OF **CASPASE** ACTIVITY
TITLE (FRENCH): TECHNIQUE DE CRIBLAGE D'AGENTS MODIFIANT LA REGULATION DE L'ACTIVITE DE LA **CASPASE**, REGULATION DANS LAQUELLE INTERVIENT LA PROTEINE INHIBITRICE DE L'APOPTOSE (IAP)
INVENTOR(S): REED, John, C.; DEVERAUX, Quinn; SALVESEN, Guy, S.; TAKAHASHI, Ryosuke; ROY, Natalie
PATENT ASSIGNEE(S): THE BURNHAM INSTITUTE
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9853091	**A1**	**19981126**

DESIGNATED STATES: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1998-US7357	19980410
PRIORITY (ORIGINAL):	US 1997-08/862087	19970522

ABEN The present invention relates to an action between an inhibitor

of apoptosis (IAP) **protein** and members of the **caspase** family of cell death **proteases** wherein the IAP regulates the activity of the **caspases**. The invention provides screening **assays** for identifying agents that alter the specific association of an IAP and a **caspase**. In addition, the invention provides methods for identifying agents that modulate the activity of a **caspase** in the presence of an IAP and that regulate the activation of a pro-**caspase** by an IAP and further provides methods of reducing the severity of a pathologic condition in an individual by administering to the individual an agent that alters the **caspase** inhibitory activity of an IAP. In addition, the invention provides methods of modulating the ability of a population of cells to survive ex vivo by contacting the cells with an agent that alters the **caspase** inhibitory activity of an IAP in the cells.

ABFR Cette invention a trait a une interaction entre une proteine inhibitrice de l'apoptose (IAP) et des membres de la famille **caspase** appartenant a la famille des **proteases** de la mort cellulaire, l'IAP regulant l'activite des **caspases**. L'invention porte sur des techniques de criblage aux fins de l'identification d'agents modifiant l'association specifique d'une IAP et d'une **caspase**. Elle concerne, de surcroit, d'une part, des methodes d'identification d'agents modulant l'activite d'une **caspase** en presence d'une IAP et regulant l'activation d'une pro-**caspase** et, d'autre part, des methodes visant a attenuer la gravite d'un etat pathologique en administrant au patient souffrant de cet etat pathologique un agent qui modifie l'activite de l'IAP, en l'occurrence, son activite inhibitrice a l'encontre de la **caspase**. Cette invention porte, en outre, sur des techniques permettant de moduler les capacites d'une population cellulaire a survivre ex vivo en mettant en contact ces cellules avec un agent modifiant l'activite inhibitrice de l'IAP a l'encontre de la **caspase** dans lesdites cellules.

L8 ANSWER 12 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent

ACCESSION NUMBER: 1998041629 PCTFULL

TITLE (ENGLISH): DEATH DOMAIN CONTAINING RECEPTOR 5

TITLE (FRENCH): RECEPTEUR 5 CONTENANT UN DOMAINE DE MORT

INVENTOR(S): NI, Jian; GENTZ, Reiner, L.; YU, Guo-Liang; SU, Jeffrey, Y.; ROSEN, Craig, A.

PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.

LANGUAGE OF PUBL.: English

LANGUAGE OF FILING: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841629	**A2**	**19980924**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-US5377 19980317

PRIORITY (ORIGINAL): US 1997-60/040846 19970317

US 1997- 19970729

ABEN The present invention relates to novel Death Domain Containing

Receptor-5 (DR5) **proteins** which are members of the tumor necrosis (TNF)
receptor family, and have now been shown to bind TRAIL. In particular, isolated nucleic acid molecules are provided encoding the human DR5 **proteins**. DR5 **polypeptides** are also provided as are vectors, host cells
and recombinant methods for producing the same. The invention further relates to screening methods for identifying antagonists and antagonists of DR5 activity.

ABFR La presente invention a trait a de nouvelles proteines de recepteur 5 contenant un domaine de mort (DR5), qui constituent des membres de la famille des recepteurs du facteur de necrose des tumeurs (TNF); il a maintenant ete demontre que ces proteines se lient au TRAIL (ligand inducteur d'apoptose lie au TNF). L'invention concerne en particulier des molecules d'acides nucleiques isolees qui codent pour les proteines DR5 humaines. L'invention concerne egalement des **polypeptides** de DR5, des vecteurs, des cellules hotes et des procedes de
recombinaison servant a produire ceux-ci. L'invention a en outre trait a des techniques de criblage permettant d'identifier des agonistes et des antagonistes de l'activite de DR5.

L8 ANSWER 13 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent

ACCESSION NUMBER:	1998041090 PCTFULL
TITLE (ENGLISH):	METHODS AND COMPOSITIONS FOR STIMULATING APOPTOSIS AND CELL DEATH OR FOR INHIBITING CELL GROWTH AND CELL ATTACHMENT
TITLE (FRENCH):	METHODES ET COMPOSITIONS DESTINEES A STIMULER L'APOPTOSE ET LA MORT CELLULAIRE OU A INHIBER LA CROISSANCE ET LA FIXATION CELLULAIRES
INVENTOR(S):	FU, Xin-Yuan; CHIN, Yue, E.; XIE, Bing
PATENT ASSIGNEE(S):	YALE UNIVERSITY
LANGUAGE OF PUBL.:	English
LANGUAGE OF FILING:	English
DOCUMENT TYPE:	Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9841090	**A1**	**19980924**

DESIGNATED STATES:	AU CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.:	WO 1998-US5307 19980319
PRIORITY (ORIGINAL):	US 1997-60/041410 19970319

ABEN The present invention relates generally to methods of modulating the rate and/or amount of a cellular process selected from the group consisting of cell growth, cell detachment and cell migration, and cellular apoptosis, said method comprising altering the RECEPTOR/PTK-STAT pathway of a cell. More particularly, the present invention relates to methods wherein the RECEPTOR/PTK-STAT pathway is altered by increasing or decreasing the amount of phosphorylated RECEPTOR/PTK-STAT **proteins** present in a cell. The present invention also relates to the
identification of agents that either promote or inhibit the phosphorylation of RECEPTOR/PTK-STAT **proteins**, as well as to the agents
themselves and to the methods which utilize such identified agents. The methods of the present invention are useful for treating mammalian diseases, including, but not limited to, cancer, autoimmune diseases, viral susceptibility, degenerative disorders, ischemic injuries, and conditions of obesity.

ABFR La presente invention concerne d'une maniere generale des methodes de modulation de la vitesse et/ou le degre de progression d'un processus cellulaire, selectionne dans le groupe constitue de la croissance cellulaire, du detachement cellulaire et de la migration cellulaire, ainsi que l'apoptose cellulaire, cette methode consistant a modifier la voie RECEPTEUR/PTK-STAT d'une cellule. Plus particulierement, la presente invention concerne des methodes dans lesquelles la voie RECEPTEUR/PTK-STAT est modifiee par augmentation ou reduction de la

quantite de proteines RECEPTEUR/PTK-STAT phosphorylees presentes dans une cellule. La presente invention concerne egalement l'identification d'agents qui soit stimulent, soit inhibent la phosphorylation de proteines RECEPTEUR/PTK-STAT, ainsi que les agents eux-memes et les methodes dans lesquelles on utilise ces agents identifies. Les methodes de la presente invention sont utiles dans le traitement de maladies mammaliennes, et notamment, mais non exclusivement, le cancer, des maladies auto-immunes, la sensibilite virale, des troubles degeneratifs, des lesions ischemiques et des etats d'obesite.

L8 ANSWER 14 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998040397 PCTFULL
TITLE (ENGLISH): BAX INHIBITOR **PROTEINS**
TITLE (FRENCH): PROTEINES INHIBITRICES DE BAX
INVENTOR(S): REED, John, C.; XU, Qunli
PATENT ASSIGNEE(S): THE BURNHAM INSTITUTE
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9840397	**A1**	**19980917**

DESIGNATED STATES: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1998-US5015 19980313
PRIORITY (ORIGINAL): US 1997-08/818514 19970314

ABEN The present invention provides substantially purified nucleic acid molecules encoding Bax inhibitor **protein**-1 (BI-1; SEQ ID NO:1) or Bax inhibitor **protein**-2 (BI-2; SEQ ID NO:4), nucleic acid molecules complementary thereto (SEQ ID NO:2 and SEQ ID NO:5, respectively), portions of such nucleic acid molecules, vectors containing the nucleic acid molecules, and host cells containing the vectors. The invention also provides methods of using such nucleic acid molecules to identify the presence of a nucleic acid molecule encoding a Bax inhibitor **protein** in a sample or to increase or decrease the level of expression of a Bax inhibitor **protein** in a cell. In addition, the invention provides substantially purified BI-1 (SEQ ID NO:3) and BI-2 (SEQ ID NO:6) **polypeptides**, portions of such **polypeptides**, and antibodies specific for BI-1 or BI-2. The invention also provides methods of using a BI-1 or BI-2 **polypeptide**, or a peptide portion thereof, to identify the presence of a member of the Bcl-2 family of **proteins** in a sample. The invention further provides methods of identifying agents that can modulate the binding of BI-1 or BI-2 to a Bcl-2 family **protein**, or that can modulate the function of BI-1 or BI-2, irrespective of its ability to bind a Bcl-2 family **protein**.

ABFR L'invention concerne des molecules d'acides nucleiques sensiblement purifiees codant pour la proteine-1 inhibitrice de Bax (BI-1; SEQ ID NO:1) ou la proteine-2 inhibitrice de Bax (BI-2; SEQ ID NO:4), des molecules d'acides nucleiques complementaires a celles-ci (SEQ ID NO:2 et SEQ ID NO:5, respectivement), des parties de telles molecules d'acides nucleiques, des vecteurs contenant les molecules d'acides nucleiques, et des cellules hotes contenant ces vecteurs. L'invention concerne egalement des procedes d'utilisation de telles molecules d'acides nucleiques pour identifier la presence d'une molecule d'acides nucleiques codant pour une proteine inhibitrice de Bax dans un echantillon, ou pour accroitre ou reduire le niveau d'expression d'une proteine inhibitrice de Bax dans une cellule. En outre, l'invention concerne des **polypeptides** de BI-1 (SEQ ID NO:3) et de BI-2 (SEQ ID NO:6) sensiblement purifies, des parties de tels **polypeptides**, et des

anticorps specifiques de BI-1 et de BI-2. L'invention concerne egalement des procedes d'utilisation d'un **polypeptide** de BI-1 ou de BI-2, ou d'une partie peptidique de celui-ci, pour identifier la presence d'un element de la famille de proteines Bcl-2 dans un echantillon. L'invention concerne en outre des procedes permettant d'identifier des agents pouvant moduler la fixation de BI-1 ou de BI-2 a une proteine de la famille des Bcl-2, ou pouvant moduler la fonction de BI-1 ou de BI-2, quelle que soit leur capacite de fixation d'une proteine de la famille des Bcl-2.

L8 ANSWER 15 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998034946 PCTFULL
TITLE (ENGLISH): DAXX, A NOVEL FAS-BINDING **PROTEIN** THAT ACTIVATES JNK AND APOPTOSIS
TITLE (FRENCH): DAXX, NOUVELLE PROTEINE FIXATRICE DE FAS ACTIVANT UNE JNK (KINASE N-TERMINALE DE JUN) ET L'APOPTOSE
INVENTOR(S): YANG, Xiaolu; KHOSRAVI-FAR, Roya; CHANG, Howard, Y.; BALTIMORE, David
PATENT ASSIGNEE(S): MASSACHUSETTS INSTITUTE OF TECHNOLOGY
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9834946	**A1**	**19980813**

DESIGNATED STATES: CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1998-US2588	19980212
PRIORITY (ORIGINAL):	US 1997-60/037919	19970212
	US 1997-60/051753	19970626
	US 1998-<none>	19980212

ABEN The invention describes nucleic acids encoding the Daxx **protein**, including fragments and biologically functional variants thereof. Also included are **polypeptides** and fragments thereof encoded by such nucleic acids, and antibodies relating thereto. Methods and products for using such nucleic acids and **polypeptides** also are provided.

ABFR L'invention concerne des acides nucleiques codant pour la proteine Daxx, y compris des fragments et des variants fonctionnels biologiques de ceux-ci. L'invention concerne egalement des **polypeptides** et des fragments de ces derniers, qui sont codes par de tels acides nucleiques, ainsi que des anticorps correspondants. L'invention concerne egalement des procedes et des produits servant a l'utilisation de tels acides nucleiques et **polypeptides**.

L8 ANSWER 16 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998034120 PCTFULL
TITLE (ENGLISH): **PROTEIN** FRAGMENT COMPLEMENTATION **ASSAYS** TO DETECT BIOMOLECULAR INTERACTIONS
TITLE (FRENCH): ANALYSES PAR COMPLEMENTATION DE FRAGMENTS PROTEIQUES POUR DETECTER DES INTERACTIONS BIOMOLECULAIRES
INVENTOR(S): MICHNICK, Stephen, William, Watson; PELLETIER, Joelle, Nina; REMY, Ingrid
PATENT ASSIGNEE(S): UNIVERSITE DE MONTREAL
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9834120	**A1**	**19980806**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH
GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT
BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-CA68 19980202
PRIORITY (ORIGINAL): CA 1997-2196496 19970131

ABEN We describe a strategy for designing and implementing **protein**-fragment complementation **assays** (PCAs) to detect biomolecular interactions in vivo and in vitro . The design, implementation and broad applications of this strategy are illustrated with a large number of enzymes with particular detail provided for the example of murine dihydrofolate reductase (DHFR). Fusion peptides consisting of N and C -terminal fragments of murine DHFR fused to GCN4 leucine zipper sequences were coexpressed in Escherichia coli grown in minimal medium, where the endogenous DHFR activity was inhibited with trimethoprim. Coexpression of the complementary fusion products restored colony formation. Survival only occurred when both DHFR fragments were present and contained leucine-zipper forming sequences, demonstrating that reconstitution of enzyme activity requires assistance of leucine zipper formation. DHFR fragment-interface point mutants of increasing severity (Ile to Val, Ala and Gly) resulted in a sequential increase in E. coli doubling times illustrating the successful DHFR fragment reassembly rather that non-specific interactions between fragments. This **assay** could be used to study equilibrium and kinetic aspects of molecular interactions including **protein-protein**, **protein**-DNA, **protein**-RNA, **protein**-carbohydrate and **protein**-small molecule interactions, for screening cDNA libraries for binding of a target **protein** with unknown **proteins** or libraries of small organic molecules for biological activity. The selection and design criteria applied here is developed for numerous examples of clonal selection, colorometric, fluorometric and other **assays** based on enzymes whose products can be measured. The development of such **assay** systems is shown to be simple, and provides for a diverse set of **protein** fragment complementation applications.

ABFR Nous decrivons une strategie permettant de creer et de mettre en oeuvre des analyses par complementation de fragments proteiques (PCA) pour detecter des interactions biomoleculaires in vivo et in vitro . La creation, la mise en oeuvre et les larges applications de cette strategie sont illustrees par un grand nombre d'enzymes, notamment par l'exemple detaille de l'hydrofolate reductase murine (DHFR). Les peptides de fusion comprenant les fragments N et C-terminaux de la DHFR murine condenses avec les sequences formant des glissieres a leucine GCN4 ont ete co-exprimees chez Escherichia coli cultivee dans un milieu minimum, chez laquelle l'activite DHFR endogene a ete inhibee par le trimethoprime. La co-expression des produits de fusion complementaires a permis de nouveau la formation de colonies. La survie n'etait possible que quand les fragments de DHFR etaient presents et contenaient des sequences formatrices de glissieres a leucine, ce qui montre que la formation de ces dernieres est necessaire a la reconstitution de l'activite enzymatique. Les mutations ponctuelles fragment DHFR-interface d'une importance croissante (Ile vers Val, Ala et Gly) ont abouti a un augmentation des temps de doublement d' E. coli , ce qui illustre la reussite du reassemblage des fragments de DHFR plutot que des interactions non specifiques entre fragments. Cette analyse a ete utilisee pour etudier l'equilibre et les aspects cinetiques des interactions moleculaires, notamment des interactions proteine-proteine, proteine-ADN, proteine-ARN, proteine-glucide et proteine-petite molecule, dans le but de cribler des librairies d'ADNc permettant de lier une proteine cible a des proteines inconnues ou des librairies de petites molecules organiques en vue d'etudier leur

activite biologique. Les criteres de selection et de creation appliques ici ont ete developpes pour de nombreux exemples d'analyses par selection clonale, d'analyses colorimetriques, fluorimetiques et autres, basees sur des enzymes dont les produits peuvent etre doses. La creation de ces systemes d'analyse, qui s'est averee simple, permet diverses applications de la complementation de fragments proteiques.

L8 ANSWER 17 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998032856 PCTFULL
TITLE (ENGLISH): DEATH DOMAIN CONTAINING RECEPTOR 4 (DR4: DEATH RECEPTOR 4), MEMBER OF THE TNF-RECEPTOR SUPERFAMILY AND BINDING TO TRAIL (APO2-L)
TITLE (FRENCH): RECEPTEUR 4 (DR4-RECEPTEUR 4 DE MORT CELLULAIRE) CONTENANT DES DOMAINES DE MORT CELLULAIRE, MEMBRE DE LA SUPERFAMILLE DU RECEPTEUR DU FACTEUR DE NECROSE TUMORALE (TNF) ET SE LIANT A LA QUEUE (APO2-L)
INVENTOR(S): GENTZ, Reiner, L.; NI, Jian; ROSEN, Craig, A.; DIXIT, Vishva, M.; PAN, James, G.
PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.; THE REGENTS OF THE UNIVERSITY OF MICHIGAN
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9832856	**A1**	**19980730**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1998-US1464	19980127
PRIORITY (ORIGINAL):	US 1997-60/035722	19970128
	US 1997-60/037829	19970205

ABEN The present invention relates to novel Death Domain Containing Receptor-4 (DR4) **proteins** which are members of the tumor necrosis factor (TNF) receptor family. In particular, isolated nucleic acid molecules are provided encoding the human DR4 **proteins**. DR4 **polypeptides** are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of DR4 activity.

ABFR L'invention concerne de nouvelles proteines receptrices (DR4) contenant des domaines de mort cellulaire appartenant a la famille des recepteurs du facteur de necrose tumorale (TNF). L'invention concerne en particulier des molecules d'acide nucleique isolees codant les proteines humaines DR4. L'invention se rapporte egalement a des **polypeptides** de DR4, ainsi qu'a des vecteurs, des cellules hotes et des procedes de recombinaison permettant de preparer lesdits **polypeptides**. Enfin, l'invention se rapporte a des procedes de criblage permettant d'identifier des agonistes et antagonistes de l'activite des proteines DR4.

L8 ANSWER 18 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1998001549 PCTFULL
TITLE (ENGLISH): GENETIC SEQUENCES AND **PROTEINS** RELATED TO ALZHEIMER'S DISEASE, AND USES THEREFOR
TITLE (FRENCH): SEQUENCES GENETIQUES ET PROTEINES LIEES A LA MALADIE D'ALZHEIMER,

ET LEURS EMPLOIS
INVENTOR(S): ST. GEORGE-HYSLOP, Peter, H.; FRASER, Paul, E.; ROMMENS, Johanna, M.
PATENT ASSIGNEE(S): THE GOVERNING COUNCIL OF THE UNIVERSITY OF TORONTO; HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9801549	**A2**	**19980115**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1997-CA475	19970704
PRIORITY (ORIGINAL):	US 1996-60/021673	19960705
	US 1996-60/021700	19960712
	US 1996-60/029895	19961108
	US 1997-60/034590	19970102

ABEN The identification, isolation, sequencing and characterization of two human presenilin genes, PS-1 and PS-2, mutations of which lead to Familial Alzheimer's Disease, are disclosed. Presenilin gene homologs in mice, C. elegans and D. melanogaster are also disclosed. Use of the nucleic acids and **proteins** comprising or derived from the presenilins in screening and diagnosing Alzheimer's Disease, identifying and developing therapeutics for treatment of Alzheimer's Disease, in producing cell lines and transgenic animals useful as models of Alzheimer's Disease. Methods for identifying substances that bind to, or modulate the activity of, a presenilin **protein**, functional fragment or variant thereof, or a mutein thereof, and methods for identifying substances that affect the interaction of a presenilin-interacting **protein** with a presenilin **protein**, functional fragment or variant thereof, or a mutein thereof, are further disclosed.

ABFR L'invention porte sur l'identification, l'isolement, le sequencage et la caracterisation de deux genes de la presenilite humaine (PS-1 et PS-2) dont certaines mutations provoquent l'affection familiale d'Alzheimer. L'invention porte aussi sur des homologues du gene de la presenilite (C. elegans et D. melanogaster) chez les souris, ainsi que sur l'utilisation d'acides nucleiques et de proteines contenant lesdits genes de la presenilite ou derives desdits genes pour rechercher et diagnostiquer la maladie d'Alzheimer, identifier et mettre au point des methodes therapeutiques destinees a traiter la maladie d'Alzheimer, produire des lignees cellulaires et des animaux transgeniques utiles comme modeles pour la maladie d'Alzheimer. L'invention concerne en outre des procedes permettant d'identifier des substances qui se lient a une proteine de la presenilite ou qui modulent l'activite d'une telle proteine, un fragment ou allele fonctionnel desdites substances ou leur muteine; l'invention concerne egalement des procedes permettant d'identifier des substances qui affectent l'action reciproque d'une proteine interagissant avec le gene de la presenilite et d'une proteine de lapresenilite, d'un fragment ou allele fonctionnel desdites substances ou leur muteine.

L8 ANSWER 19 OF 21 PCTFULL COPYRIGHT 2001 MicroPatent
ACCESSION NUMBER: 1997045533 PCTFULL
TITLE (ENGLISH): ENGINEERING ORAL TISSUES
TITLE (FRENCH): RECONSTITUTION DE TISSUS BUCCAUX
INVENTOR(S): MOONEY, David, J.; RUTHERFORD, Robert, Bruce
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF MICHIGAN
LANGUAGE OF PUBL.: English
LANGUAGE OF FILING: English

DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9745533	**A1**	**19971204**

DESIGNATED STATES: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US8977 19970528
PRIORITY (ORIGINAL): US 1996-60/018450 19960528

ABEN Disclosed are methods for regenerating dental and oral tissues from viable cells using ex vivo culture on a structural matrix. The regenerated oral tissues and tissuematrix preparations thus provided have both clinical applications in dentistry and oral medicine and are also useful in in vitro toxicity and biocompatibility testing.

ABFR L'invention porte sur une methode de regeneration de tissus dentaires et buccaux a partir de cellules viables en culture ex vivo sur des matrices structurelles. Les tissus buccaux regeneres et les preparations tissu/matrice ainsi obtenues ont des applications en medecine dentaire et orale et peuvent egalement servir pour des tests in vitro de toxicite et de biocompatibilite.

L8 ANSWER 20 OF 21 USPATFULL
ACCESSION NUMBER: 1999:36949 USPATFULL
TITLE: Engineering oral tissues
INVENTOR(S): Mooney, David J., Ann Arbor, MI, United States
Rutherford, Robert B., Ann Arbor, MI, United States
PATENT ASSIGNEE(S): The Regents of the University of Michigan, Ann Arbor, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5885829		19990323	<--
APPLICATION INFO.:	US 1997-864494		19970528	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-18450	19960528	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Degen, Nancy
LEGAL REPRESENTATIVE: Arnold, White & Durkee
NUMBER OF CLAIMS: 109
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT: 8001
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods for regenerating dental and oral tissues from viable cells using ex vivo culture on a structural matrix. The regenerated oral tissues and tissue-matrix preparations thus provided have both clinical applications in dentistry and oral medicine and are also useful in in vitro toxicity and biocompatibility testing.

L8 ANSWER 21 OF 21 USPATFULL
ACCESSION NUMBER: 1998:144234 USPATFULL
TITLE: Bax inhibitor proteins
INVENTOR(S): Reed, John C., Rancho Santa Fe, CA, United States
Xu, Qunli, La Jolla, CA, United States
PATENT ASSIGNEE(S): The Burnham Institute, La Jolla, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5837838		19981117	<--

APPLICATION INFO.: US 1997-818514 19970314 (8)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Scheiner, Toni R.
LEGAL REPRESENTATIVE: Campbell & Flores LLP
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1,4
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 2101
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides substantially purified nucleic acid molecules encoding Bax inhibitor protein-1 (BI-1; SEQ ID NO: 1) or Bax inhibitor protein-2 (BI-2; SEQ ID NO: 4), nucleic acid molecules complementary thereto (SEQ ID NO: 2 and SEQ ID NO: 5, respectively), portions of such nucleic acid molecules, vectors containing the nucleic acid molecules, and host cells containing the vectors. The invention also provides methods of using such nucleic acid molecules to identify the presence of a nucleic acid molecule encoding a Bax inhibitor protein in a sample or to increase or decrease the level of expression of a Bax inhibitor protein in a cell. In addition, the invention provides substantially purified BI-1 (SEQ ID NO: 3) and BI-2 (SEQ ID NO: 6) polypeptides, portions of such polypeptides, and antibodies specific for BI-1 or BI-2. The invention also provides methods of using a BI-1 or BI-2 polypeptide, or a peptide portion thereof, to identify the presence of a member of the Bcl-2 family of proteins in a sample. The invention further provides methods of identifying agents that can modulate the binding of BI-1 or BI-2 to a Bcl-2 family protein, or that can modulate the function of BI-1 or BI-2, irrespective of its ability to bind a Bcl-2 family protein.